[CONTRIBUTION NO. 1386 FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

The Preparation of 1,3-Diamino-2,4-diphenylcyclobutane and Related Compounds from α-Truxillic Acid

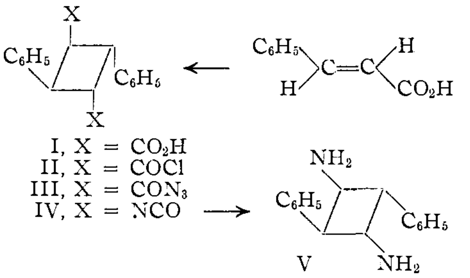
BY EMIL H. WHITE AND HARMON C. DUNATHAN

RECEIVED JULY 20, 1956

α-Truxillic acid, prepared by the photodimerization of cinnamic acid, was converted into 1,3-diamino-2,4-diphenylcyclobutane (V) by means of the Curtius reaction. The diacetyl derivative of this amine was dehydrated to form the diisoquinolinocyclobutane VII. The latter compound was found to dissociate into 1-methylisoquinoline at a temperature of *ca.* 185°.

The synthesis of 1,3-diamino-2,4-diphenylcyclobutane (V), required for a study of the deamination of aliphatic amines,[1] is reported in this paper. The synthesis of this diamine V from α-truxillic acid[2] (I) is outlined in Chart I. Although a number of compounds related to α-truxillic acid have been converted into the respective monoaminocyclobutanecarboxylic acids,[3] none have previously been converted into diaminocyclobutane derivatives.

CHART I



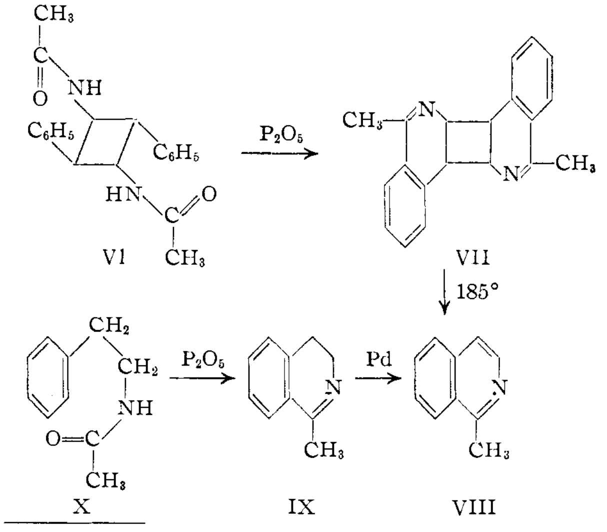
α-Truxillic acid was prepared by the photodimerization of cinnamic acid; both sunlight and artificial light[4] were used. The use of sunlight was found to be more convenient; however, a more rapid dimerization was obtained with artificial light. The photodimerization of cinnamic acid has been studied rather extensively by various workers in their attempts to synthesize the truxillic and truxinic acids. Although α-truxillic acid is the usual product of this reaction, the formation of isomers occasionally has been reported.[4,5] During the course of our work, only α-truxillic acid was isolated from the dimerizations; our attempts to find isomeric acids were unsuccessful.

α-Truxillic acid was converted into 1,3-diamino-2,4-diphenylcyclobutane (V) by means of the sodium azide modification of the Curtius reaction.[6] The hydrazide modification was used initially, but later abandoned because of difficulties encountered in preparing the hydrazide. Single attempts to utilize the Hofmann[6] and the Schmidt[6] reactions were unsuccessful.

Truxillyl chloride (III) was obtained from the reaction of the acid I with thionyl chloride. It was purified carefully since crude preparations yielded, in part, an azide which did not readily form the isocyanate. Hydrolysis of the pure acid chloride yielded only the α-isomer of truxillic acid.

The reaction of II with sodium azide proceeded very slowly in refluxing ether or benzene, but readily at 0° in alcohol-free chloroform. During the course of this reaction, the azide III decomposed partially into the isocyanate IV; the process was completed by refluxing the solution (after the acid chloride had reacted completely). The isocyanate reacted with ethanol to form the urethan, but it did not react with benzoic acid, even in the presence of hydrogen chloride. The isocyanate was hydrolyzed to the amine V with a mixture of dilute hydrochloric acid and dioxane. An over-all yield of 60% of the pure amine was obtained from the acid chloride II. The amine is assumed to have the structure and the *trans–trans* configuration shown (chart I), since the Curtius reaction has been shown to proceed without isomerization and with retention of configuration in a number of related cases.[7] Furthermore, the spectra and the physical properties are consistent with structure V. The gross structure of the amine was confirmed by the sequence of reactions shown in Chart II.

CHART II



---

(1) E. H. White, THIS JOURNAL, **77**, 6011 (1955).

(2) For a general discussion of the structure and stereochemistry of α-truxillic acid, see R. H. Rodd, "Chemistry of Carbon Compounds," Elsevier Publishing Co., New York, N. Y., 1953, p. 61.

(3) *E.g.*, R. Stoermer and W. Keller, *Ber.*, **64**, 2783 (1931); H. I. Bernstein and E. S. Wallis, *J. Org. Chem.*, **7**, 261 (1942).

(4) A 275 watt General Electric Sun Lamp was our source. Stobbe and Lehfeldt (*Ber.*, **58**, 2415 (1925)) used a quartz ultraviolet lamp in some of their experiments; they showed that the light from this source was capable not only of dimerizing the cinnamic acid, but also of depolymerizing the dimeric acids. Other workers have used sunlight for the dimerizations.

(5) H. I. Bernstein and W. C. Quimby, THIS JOURNAL, **65**, 1845 (1943).

(6) "Organic Reactions," Vol. III. John Wiley and Sons, Inc., New York, N. Y., 1946.

(7) E. R. Buchman, A. O. Reims, T. Skei and M. J. Schlatter, THIS JOURNAL, **64**, 2696 (1942); O. Diels, Blom and Koll, *Ann.*, **443**, 246, 257 (1925); A. Campbell and J. Kenyon, *J. Chem. Soc.*, **148**, 25 (1946).

The diacetyl derivative of the amine VI was converted into 6a,6b,12a,12b-tetrahydro-5,11-dimethylcyclobuta[1,2-*c*,3,4-*c′*]diisoquinoline (VII) by means of the Bischler–Napieralski reaction.[8] The structure of VII follows from the method of synthesis; the structure is consistent with the spectra and with the physical and chemical properties of VII. During the course of this synthesis, it was observed that the melting points of VII varied with the rate of heating; furthermore, a spectroscopic examination of the melt indicated that a new compound was formed at the melting point. Air oxidation was ruled out when similar results were obtained in an evacuated system. The new compound was more highly conjugated than VII and it seemed likely that thermal cleavage to an isoquinoline had occurred. Subsequently, the controlled decomposition of VII at 185° yielded 80% by weight of the new compound, which proved to be identical with a sample of 1-methylisoquinoline (VIII) prepared by an independent route (Chart II).[9]

Experimental[10]

α-Truxillic Acid (I).—Three hundred grams of cinnamic acid[11] (m.p. 132–133°) was suspended in 10 liters of water in a Pyrex round-bottom flask containing a cooling coil and a stirrer. Three 275 watt sun lamps[12] were placed within 1 cm. of the flask. After seven days of irradiation, the solid was filtered, dried, and extracted with ether in a Soxhlet apparatus for *ca.* one day. The non-extracted material weighed 34.6 g., m.p. 280–283°. This was recrystallized from acetic acid to yield 28.3 g. (9.5%) of white crystals, m.p. 283–284°. (lit.[13] 285°), infrared spectrum C═O (5.86 and 5.91 μ in KBr); methyl ester, m.p. 176–177° (lit.[14] 174–175°), infrared spectrum, C═O (5.78 μ in $CHCl_3$); ethyl ester, m.p. 149–150° (lit.[15] 146°), infrared spectrum C═O (5.77 μ in $CHCl_3$); amide, m.p. 273–274° (lit.[16] 267°).

In a typical sunlight experiment, cinnamic acid in a soft glass flask was exposed for ten winter weeks; the acid was stirred weekly. The product was worked up as before to yield 22% of recrystallized α-truxillic acid, m.p. 283.5–284.5°. A 29% yield was obtained from acid exposed for 17 weeks.

The experiments of Bernstein[5] were repeated, except that the product was worked up as we have described under truxillic acid. In each case, only α-truxillic acid was obtained. In one experiment, the total product (ten weeks exposure to sunlight of cinnamic acid from Antoine Chiris Co.) was converted into the mixed methyl esters with methanol and hydrogen chloride (95% yield). The product was chromatographed on neutral alumina; only methyl cinnamate and methyl α-truxillate were obtained (identified by m.p. and infrared spectrum).

α-Truxillyl Chloride (II).—A suspension of the acid (5.2 g., 0.0176 mole) in 50 ml. of thionyl chloride (Eastman Kodak Co., White Label) containing a drop of dimethylaniline was refluxed for 90 minutes. The thionyl chloride was then distilled from the clear solution and the last traces were removed at 0.1 mm. Recrystallization of the product from benzene–hexane mixtures yielded 5.27 g. (0.0158 mole, 91%) of the chloride in the form of large prisms, m.p. 127.1–127.8° (lit.[13] 125°), infrared spectrum C═O (5.60 μ in $CHCl_3$).

Anal. Calcd. for $C_{18}H_{14}O_2Cl_2$: C, 64.86; H, 4.23. Found: C, 64.86; H, 3.86.

Hydrolysis of the acid chloride (0.30 g., 1.8 mmoles) in aqueous dioxane at 25° for one day yielded α-truxillic acid (0.27 g., 1.8 mmoles), m.p. 283–285°.

1,3-Diamino-2,4-diphenylcyclobutane (V).—α-Truxillyl chloride (0.723 g., 2.17 mmoles) and sodium azide[17] (0.95 g., 15 mmoles) were stirred in alcohol-free chloroform[18] at 0° for 15 hours under an atmosphere of nitrogen. The infrared spectrum at this point showed the azide band (4.68 μ) and the isocyanate band (4.43 μ) in the ratio of *ca.* 1/3, but no acid chloride bands. The solution was allowed to warm to room temperature for 5 hours, then refluxed for an hour. The infrared spectrum at this point contained only the isocyanate bands. Preparations from impure acid chloride contained *ca.* 10% of an azide which did not rearrange on prolonged refluxing. The solution was next filtered and the chloroform removed to yield 0.603 g. (2.08 mmoles, 96%) of a viscous oil.

The oil was dissolved in 150 ml. of purified dioxane[19] and 100 ml. of aqueous hydrochloric acid (1/1) was added rapidly with vigorous stirring. After five hours (under nitrogen), the solution was extracted with chloroform, the aqueous phase was made basic and then extracted with ether. The ether solution was dried (Na_2SO_4) and the ether removed. The residue (0.36 g.) was short-path distilled at 100° and 1 mm. to yield 0.310 g. (1.3 mmoles, 60% based on II) of the diamine, m.p. 2–5°.

Anal. Calcd. for $C_{16}H_{18}N_2$: C, 80.63; H, 7.61; N, 11.76. Found: C, 80.70; H, 7.45; N, 11.81.

The dibenzoate salt was prepared by mixing chloroform solutions of the reactants. Recrystallization from ethanol yielded plates, m.p. 200.5–200.8° (evacuated capillary).

Anal. Calcd. for $C_{30}H_{30}O_4N_2$: C, 74.66; H, 6.27; N, 5.81. Found: C, 74.81; H, 5.99; N, 5.73.

The dipicrate was prepared from ethanolic solutions of the reactants. Recrystallization from ethanol yielded prisms, m.p. 210–211° (evacuated capillary).

The diamine and its salts are readily air-oxidized; the latter have sharp, high melting points only in the absence of air.

Attempted Curtius Degradation *via* the Hydrazide.—A mixture of methyl truxillate and an excess of hydrazine (Mathieson, anhydrous) was refluxed for seven hours. The infrared spectrum of the product indicated a very complex mixture of hydrazides. The reaction was repeated using absolute ethanol as the solvent; refluxing for one day yielded methyl truxillate (*ca.* 50%) and a mixture of hydrazides, m.p. 185–204° (*ca.* 50%). Repetition of the latter experiment in refluxing propanol yielded a crude hydrazide, which after two recrystallizations from ethanol was obtained in the form of white crystals, m.p. 204–206°, infrared spectrum C═O (6.04 μ in Nujol).

Anal. Calcd. for $C_{18}H_{20}N_4O_2$: C, 66.65; H, 6.21; N, 17.27. Found: C, 66.93; H, 6.34; N, 17.52.

The reaction of this hydrazide with nitrous acid yielded an azide which rearranged readily to give an isocyanate; the infrared spectrum of this material and that of a specimen prepared by the sodium azide method were identical. The isocyanate did not react with benzoic acid in refluxing benzene with or without a catalytic amount of hydrogen chloride. In refluxing ethanol, it was readily converted into the diurethan, m.p. 157–159°, infrared spectrum C═O (5.85 μ in $CHCl_3$).

1,3-Diacetamido-2,4-diphenylcyclobutane (VI).—The amine V (1.94 g., 8.15 mmoles) was dissolved in 25 ml. of glacial acetic acid and 2.10 g. (21 mmoles) of acetic anhydride was added. The solution was heated to 60° for two hours, then poured into 300 ml. of ice-water and neutralized. The resulting white precipitate was filtered, dried, and recrystallization from methanol yielded **1**.99 g. (6.18

---

(8) "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 74.

(9) A literature search revealed several other cases in which cyclobutane derivatives underwent thermal cleavage; H. Stobbe and F. Zschoch, *Ber.*, **60**, 462 (1927); R. Stoermer and E. Asbrand, *ibid.*, **64**, 2796 (1931); M. Pailer and U. Muller, *Monatsh.*, **79**, 615 (1948).

(10) Melting points uncorrected.

(11) Eastman Kodak Co. or Antoine Chiris Co.

(12) General Electric, "R.S" type.

(13) R. Stoermer and G. Foerster, *Ber.*, **52**, 1263 (1919).

(14) A. W. K. de Jong, *ibid.*, **56**, 826 (1923).

(15) C. Lieberman, *ibid.*, **21**, 2346 (1888).

(16) R. Stoermer, C. Wegner and A. Carl, *ibid.*, **56**, 1690 (1923).

(17) Some samples of commercial sodium azide were found to be active in this reaction, others inactive. Occasionally, an active sample would become inactive. All inactive samples were reactivated by the procedure of E. Waltmann (*C. A.*, **36**, 2096 (1942)). The acid chloride–sodium azide reaction was carried out at 0° since, at higher temperatures, the azide occasionally became inactive during the course of a run.

(18) L. F. Fieser, "Experiments in Organic Chemistry," 3rd Ed., D. C. Heath and Co., Boston, Mass., 1955, p. 283.

(19) Footnote 18, p. 285.

mmoles, 76%) of white needles, m.p. 251–252°, infrared spectrum C=O (5.96 μ in $CHCl_3$).

Anal. Calcd. for $C_{20}H_{22}N_2O_2$: C, 74.50; H, 6.88; N, 8.69; mol. wt., 322.4. Found: C, 74.66; H, 6.76; N, 8.54; mol. wt., 330 (Rast).

Isoquinoline Dimer (VII).—1,3-Diacetamido-2,4-diphenylcyclobutane (0.95 g., 2.95 mmoles) was dissolved in 50 ml. of redistilled tetralin and 7.4 g. (52.8 mmoles) of P_2O_5 was added. The mixture was heated slowly to 160° with stirring. After heating at 160° for ten minutes, the mixture was cooled and a second 7.4-g. portion of P_2O_5 was added. The flask was reheated and kept at 160° for 30 minutes, then allowed to cool to room temperature. The tetralin was decanted and the residue was cautiously decomposed with water (*ca.* 250 ml.). The remaining tetralin was removed by steam distillation, and the aqueous phase was filtered and neutralized. The white precipitate was filtered and dried (0.640 g., 2.24 mmoles, 77%). Recrystallization from benzene yielded crystals melting between 190 and 205°, depending on the rate of heating; λ_{max} 221 mμ (log ε 4.59) and 248 mμ (log ε 4.13) in 95% ethanol.

Anal. Calcd. for $C_{20}H_{18}N_2$; C, 83.88; H, 6.34; N, 9.78; mol. wt., 286.4. Found: C, 83.84; H, 6.07; N, 9.88; mol. wt., 280 (Rast).

When the dimer VII was heated in a sublimator at *ca.* 185° and 60 mm., 1-methylisoquinoline distilled as a clear oil, m.p. 10–12°. The ultraviolet absorption spectrum in 95% ethanol had maxima at the following wave lengths (mμ, log ε in parentheses): 217 (4.79), 263 (360), 271 (3.66), 283 (3.55), 309 (3.43), 318 (3.40), 322 (3.55). The infrared spectrum of this material and that of a sample prepared from 1-methyl-3,4-dihydroisoquinoline were superimposable in detail.

The 1-methylisoquinoline from the thermal cleavage of 24.5 mg. (0.086 mmole) of the dimer, was converted into the picrate (51.8 mg., 0.139 mmole, 81%), m.p. 225–226° (lit.[20] 225–226°).

1-Methyl-3,4-dihydroisoquinoline (IX).—N-(2-Phenylethyl)-acetamide[21] (X) was converted into 1-methyl-3,4-dihydroisoquinoline in 79% yield by the method of Späth[20]; λ_{max} 210 mμ (log ε 4.27), 250 mμ (log ε 3.81) in 95% ethanol.

The picrate prepared in and recrystallized from ethanol melted at 191–194° (lit.[20] 188–190°).

1-Methylisoquinoline (VIII).—A mixture of the dihydroisoquinoline IX (0.51 g., 3.51 mmoles) and 0.122 g. of palladium black in redistilled *p*-xylene (3.5 ml.) was refluxed for three hours. The properties of the product at this point indicated only partial dehydrogenation. Fresh catalyst (0.12 g.) and xylene (4 ml.) were added to the organic material and the mixture was refluxed for another 18 hours. The catalyst was filtered, the xylene removed and the product distilled to yield 0.45 g. of a clear oil (3.12 mmole, 89%), m.p. 10–12° (lit.[22] 10.1–10.4°). The ultraviolet absorption spectrum in 95% ethanol of a sample purified *via* the picrate, had the following maxima (mμ, log ε in parentheses): 217 (4.80), 262 (3.61), 270 (3.66), 307 (3.45), 283 (3.56), 316 (3.41), 320 (3.57). The picrate melted at 224–227° (lit.[20] 225–226°).

---

[20] E. Späth, F. Berger and W. Kuntara, *Ber.*, **63**, 137 (1930).

[21] A. Michaelis and E. Linow, *ibid.*, **26**, 2167 (1893).

[22] E. Jantzen, Dechema-Monographie, No. 48, Berlin, 1932, p. 135.

NEW HAVEN, CONNECTICUT

[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY AT CORNELL UNIVERSITY]

1,2-Dimethylenecyclopentane and 1,2-Dimethylene-3-methylcyclopentane[1]

BY A. T. BLOMQUIST, JOSEPH WOLINSKY, Y. C. MEINWALD AND D. T. LONGONE

RECEIVED MAY 29, 1956

1,2-Dimethylenecyclopentane and its 3-methyl homolog have been obtained by the thermal decomposition of 1,2-bis-(dimethylaminomethyl)-cyclopentane dimethohydroxide and the like 3-methyl derivative, respectively. These dienes were also obtained, but less satisfactorily, by pyrolysis of the requisite 1,2-bis-(acetoxymethyl)-cyclopentanes. The syntheses of the precursors for the dienes involved standard classical transformations starting with the appropriate 1,2-cyclopentanedicarboxylic acids. The structures of the two dienes were confirmed by all of their observed chemical and physical properties, including their infrared and ultraviolet spectra. Both dienes formed Diels–Alder adducts with great ease and those obtained with maleic anhydride could be degraded to 2,3-hydrindene and 1-methyl-2,3-hydrindene. Persulfate initiated polymerization of the dienes at 50° for 24 hr. gave rubber-like soluble polymers comprising essentially only 1,4-addition polymerization units as indicated by their infrared spectra.

The observation that persulfate-initiated polymerization of 1,2-dimethylenecyclobutane affords a soluble, tough, elastic, rubber-like polymer[2] encouraged us to examine the properties of certain conjugated exocyclic dienes of larger carbocycles. In particular, it seemed pertinent to make a careful study of 1,2-dimethylenecyclopentane (I) and its 3-methyl homolog II. Since structural studies of 1,2-dimethylenecyclobutane polymer indicated that it comprised *ca.* 80% *cis*-1,4-units, it might be expected that under comparable polymerization conditions the dimethylenecyclopentanes should give polymers having a higher content of *cis*-1,4-units as there is considerably less "steric strain" attendant in a five-membered ring than in a four-membered ring.

In this study it also seemed desirable to examine the methods of acetate pyrolysis and Hofmann elimination with the object of determining which is better for obtaining dienes of highest purity. Inasmuch as it had been observed earlier that pyrolysis of 1,2-bis-(acetoxymethyl)-cyclobutane proceeded abnormally, possibly *via* 1,4-transannular elimination with resulting ring cleavage to form 2-vinyl-1,3-butadiene,[2,3] it was of interest to observe whether pyrolysis of the bis-acetoxymethyl cyclopentanes might also result in the formation of undesirable accessory products and hence be inferior to the Hofmann method as a route to pure exocyclic conjugated dienes.

1,2-Dimethylenecyclopentane (I).—The synthesis of I by pyrolysis of 1,2-bis-(acetoxymethyl)-cyclopentane has been described by Bailey and Sorenson,[4] but some of the properties reported for it, notably the b.p. and ultraviolet absorption spectrum, are at variance with what might be expected

---

[1] The work reported here was done as part of a general research program in organic chemistry at Cornell University sponsored by the B. F. Goodrich Co.

[2] A. T. Blomquist and J. A. Verdol, THIS JOURNAL, **77**, 1806 (1955).

[3] W. J. Bailey, C. H. Curov and L. Nicholas, *ibid.*, **77**, 2787 (1955).

[4] W. J. Bailey and W. R. Sorenson, *ibid.*, **76**, 5421 (1954).